

The Strategy Behind A Lifespan Screen

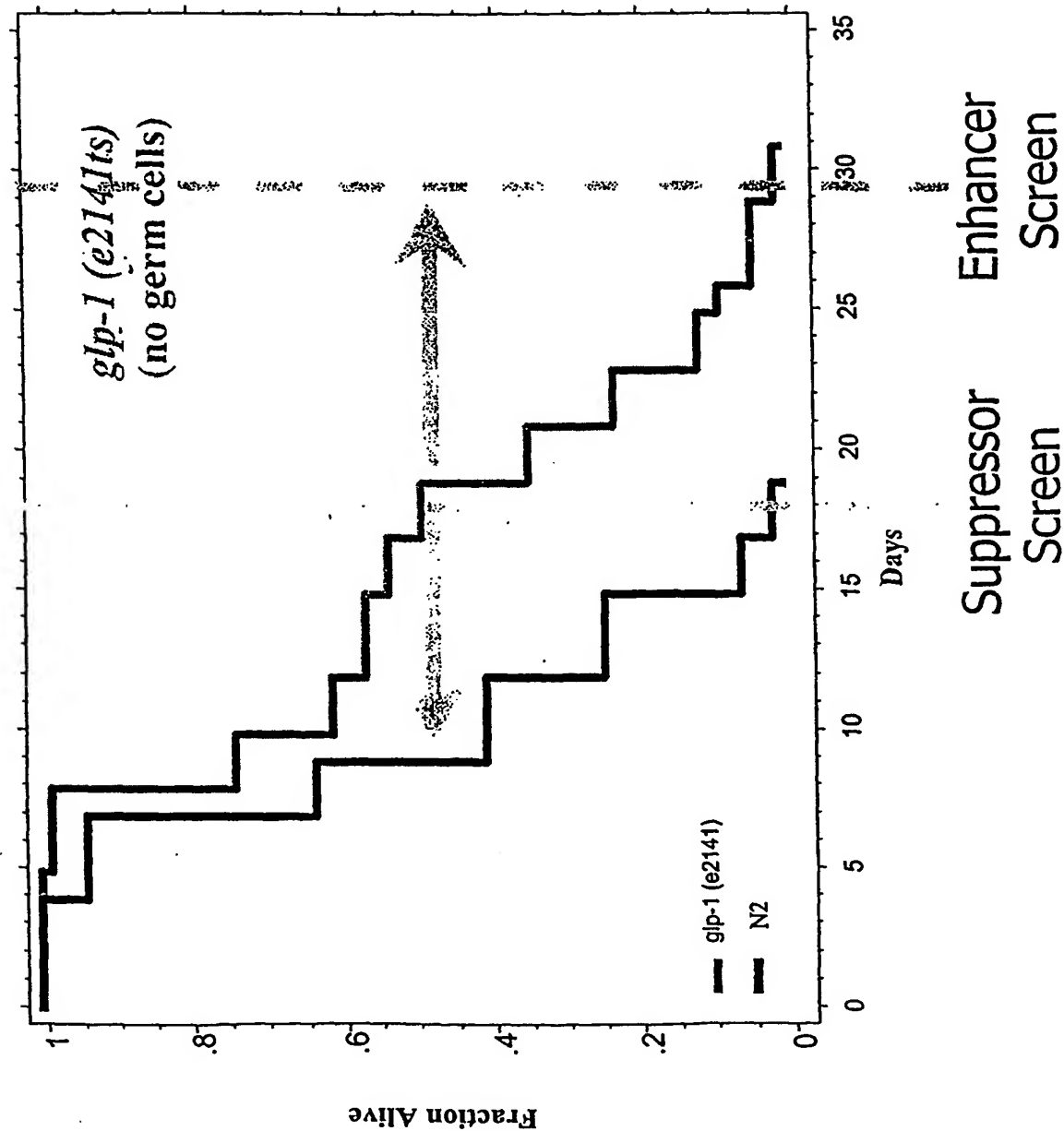


Figure 1

An Insulin Signaling Pathway and Signals from the Reproductive System Regulate Lifespan in *C. elegans*

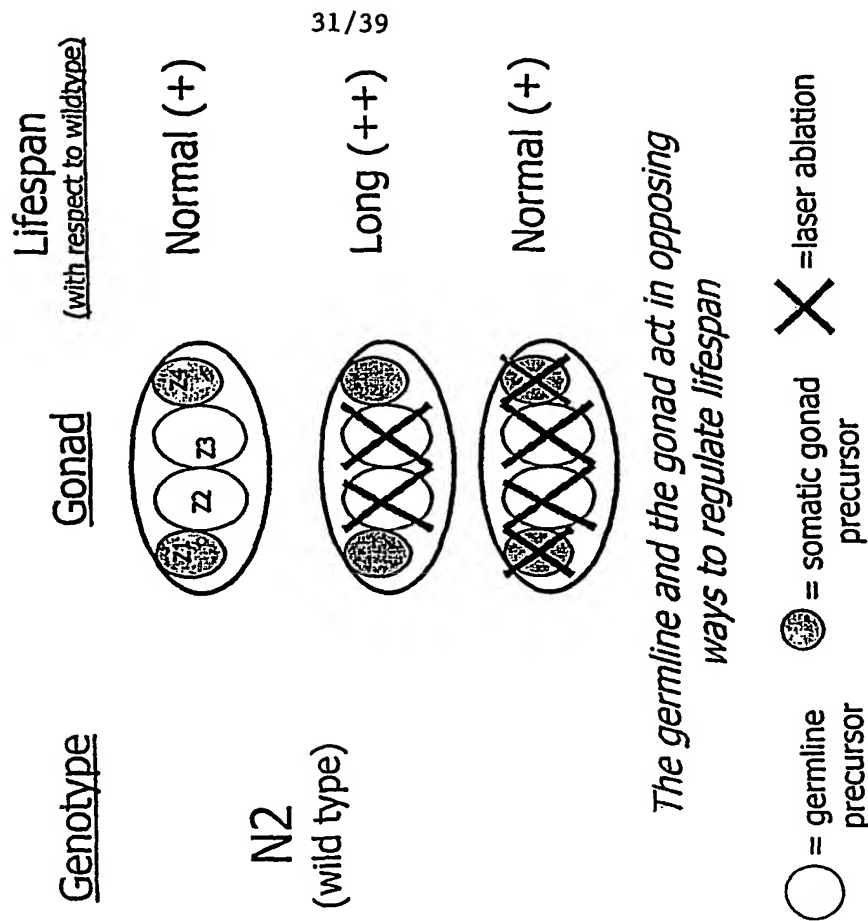
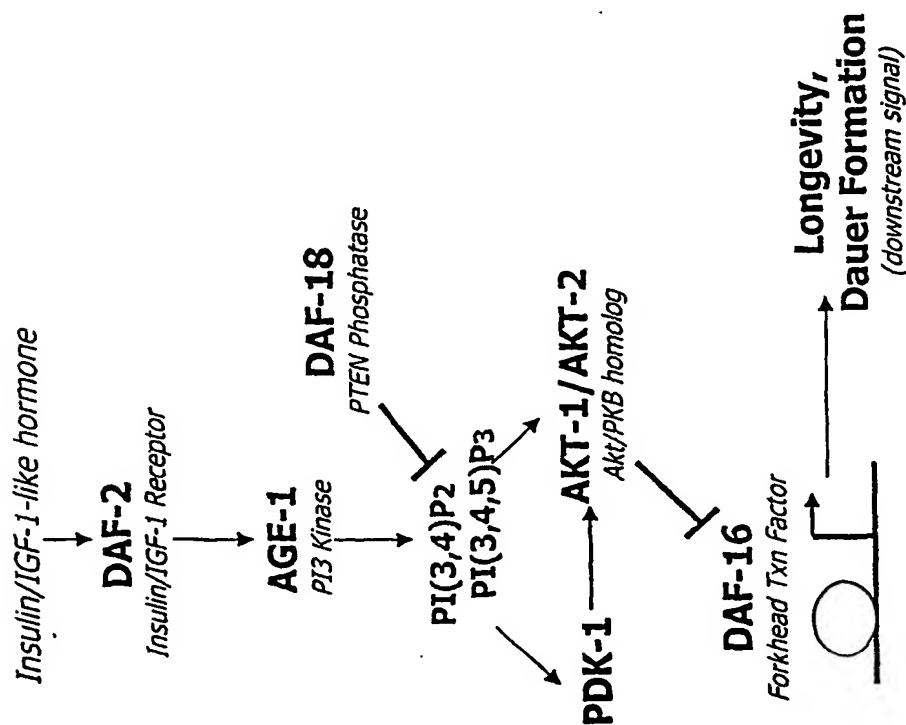

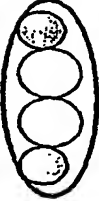


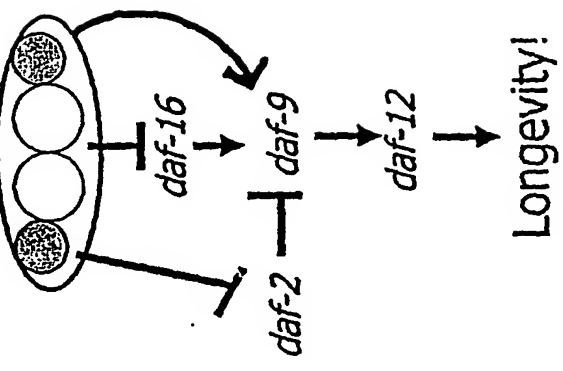


Figure 2

The Reproductive System Modulates Several Genes to Control Aging

Genotype	Gonad	Lifespan (with respect to wildtype)
<i>daf-16(-)</i> or <i>daf-12(-)</i> or <i>daf-9(-)</i>		Short (-) [no change]
The germline signal shortens lifespan through downregulation of <i>daf-16</i> , <i>daf-12</i> , and <i>daf-9</i>		
Genotype	Gonad	Lifespan (with respect to wildtype)
<i>daf-2(-)</i> [strong alleles]		Long (++)
<i>daf-2(-)</i> [strong alleles]		Even Longer (++++)
<i>daf-2(-)</i> [strong alleles]		Even Longer (++++)
The somatic gonad, but not the germline, extends life through modulation of the <i>daf-2</i> insulin pathway.		

One possible model:



What other genes are involved in this process?

Figure 3

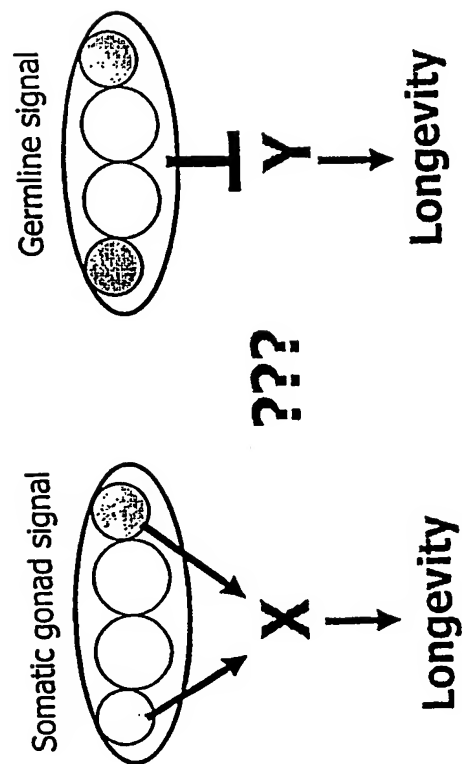
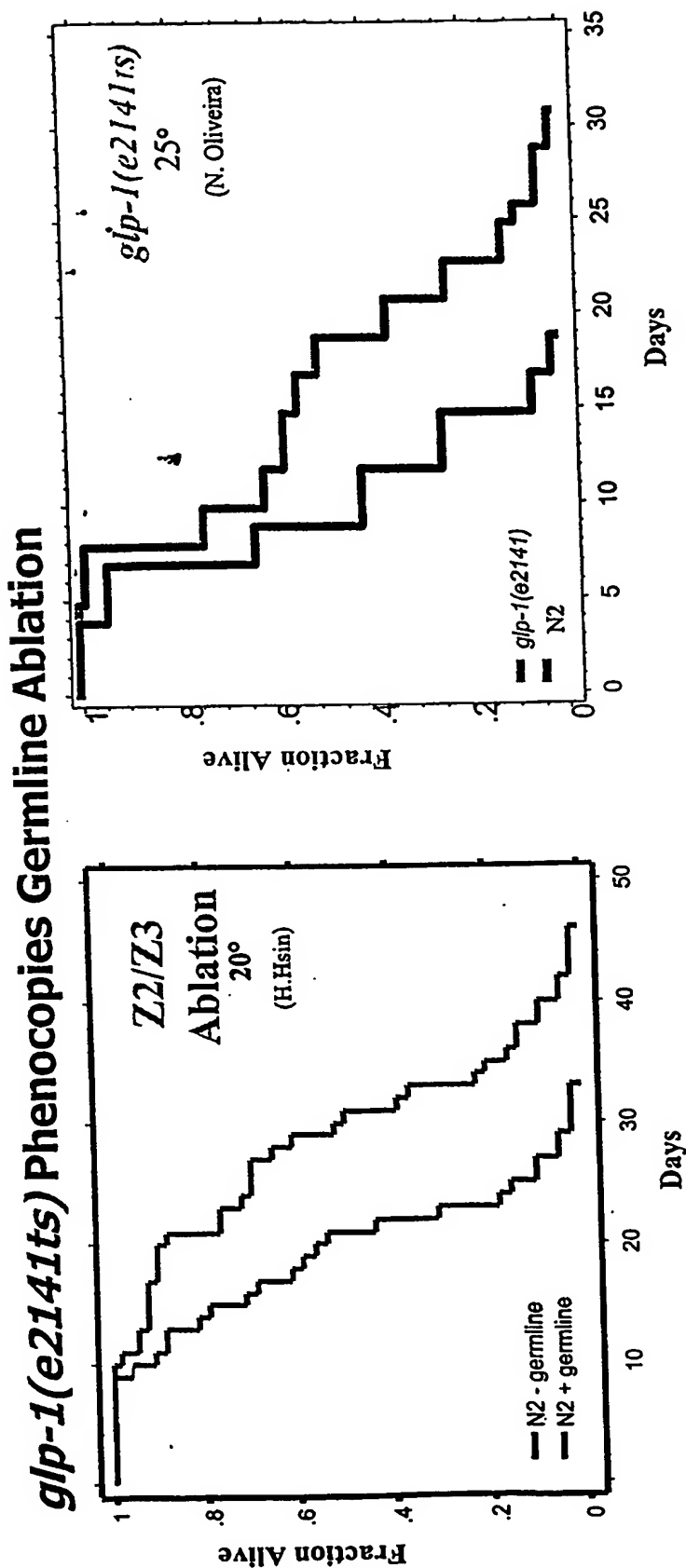
The somatic gonad signal acts through *daf-12* and *daf-9*, yet independently of *daf-16*, to promote longevity.

An RNAi Screen for Suppressors and Enhancers of *glp-1* Lifespan Extension

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Why screen?
To identify novel members of the germline, somatic gonad, and other pathways.

Figure 4

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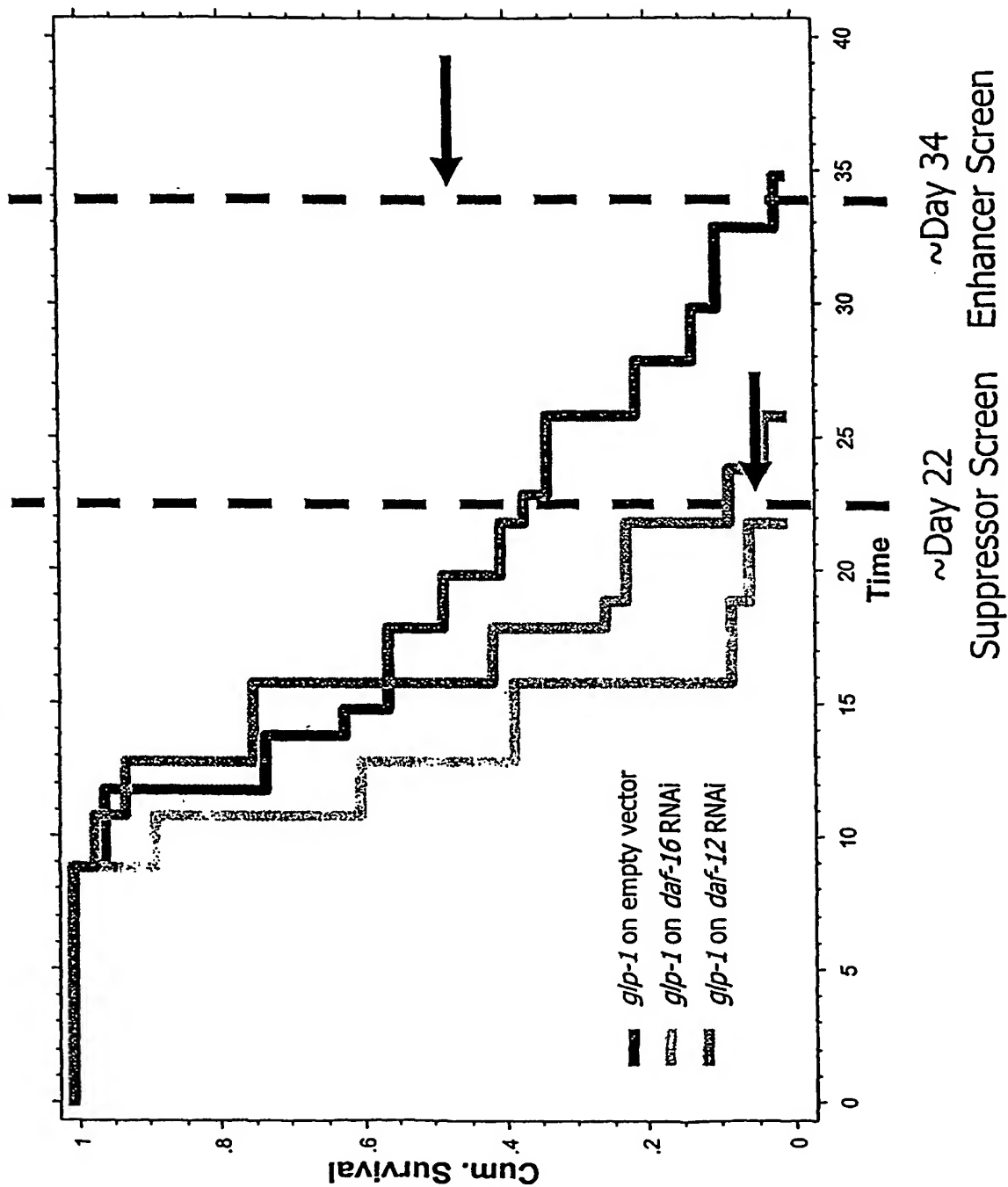
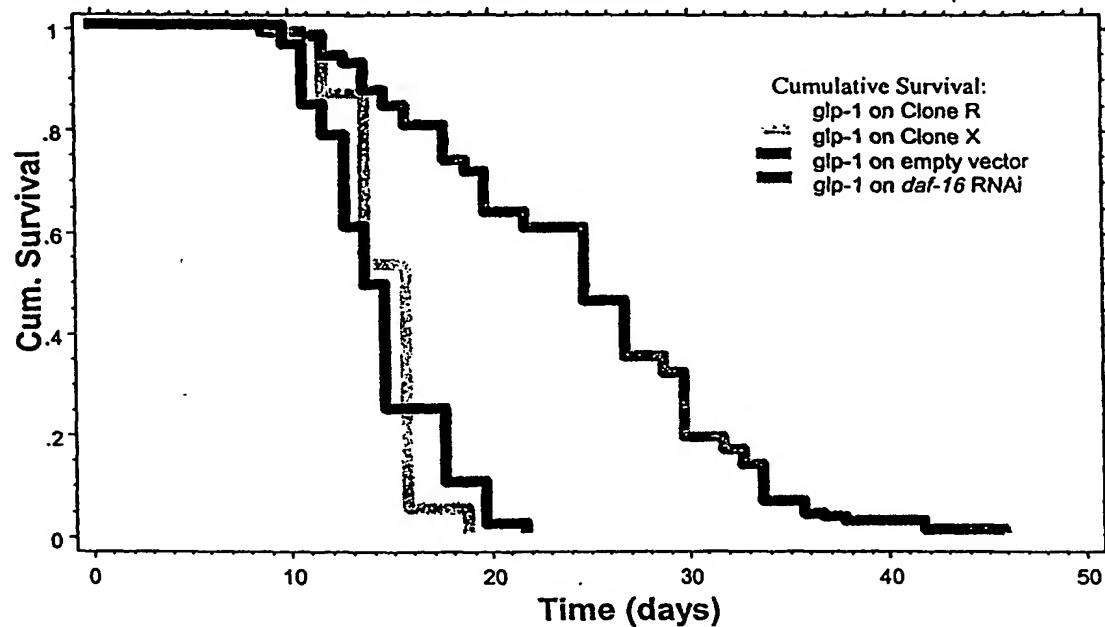
Strategy for the *glp-1* screen

Figure 5

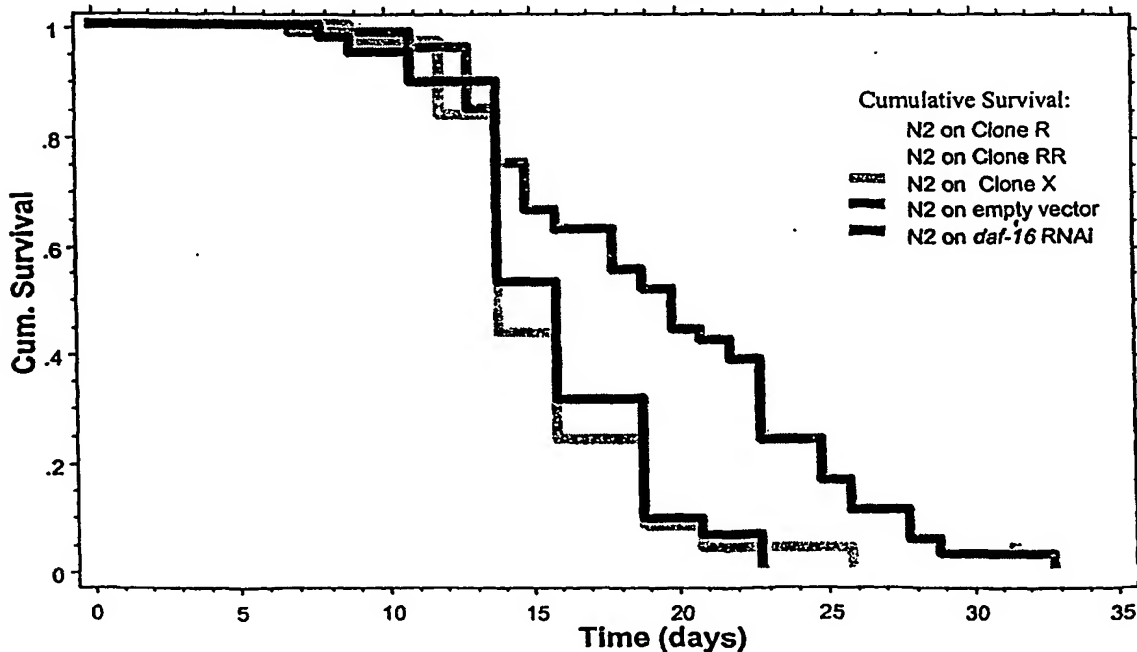
Establishing Specificity: Effects on N2 Longevity

Examples of *glp-1* suppressors:



RNAi Clone R and Clone X suppress *glp-1* longevity to *daf-16* levels

Differential effects on N2 longevity:

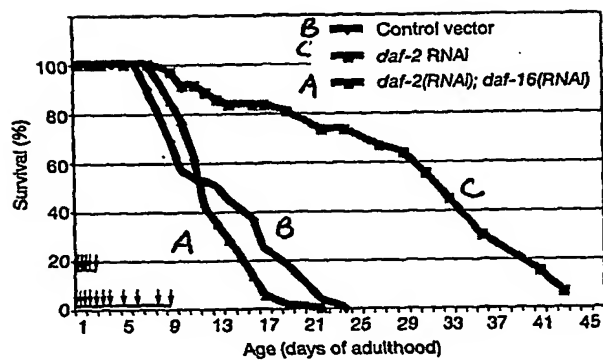


Clone R has no effect on N2 lifespan, and Clone X slightly suppresses wild-type longevity to *daf-16* levels. Clone RR dramatically reduces N2 lifespan,

Figure 6

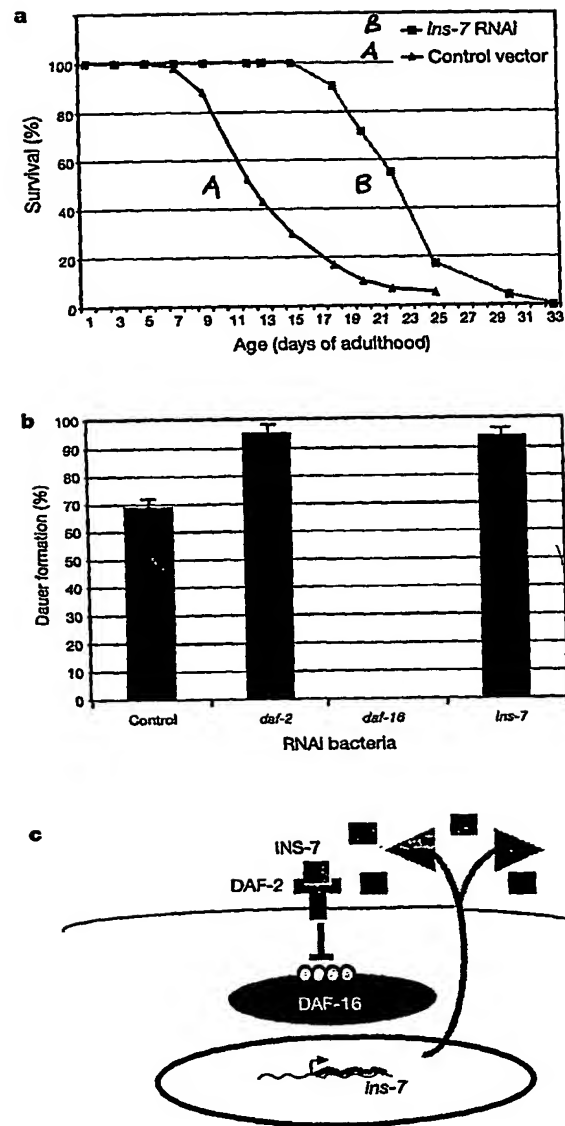
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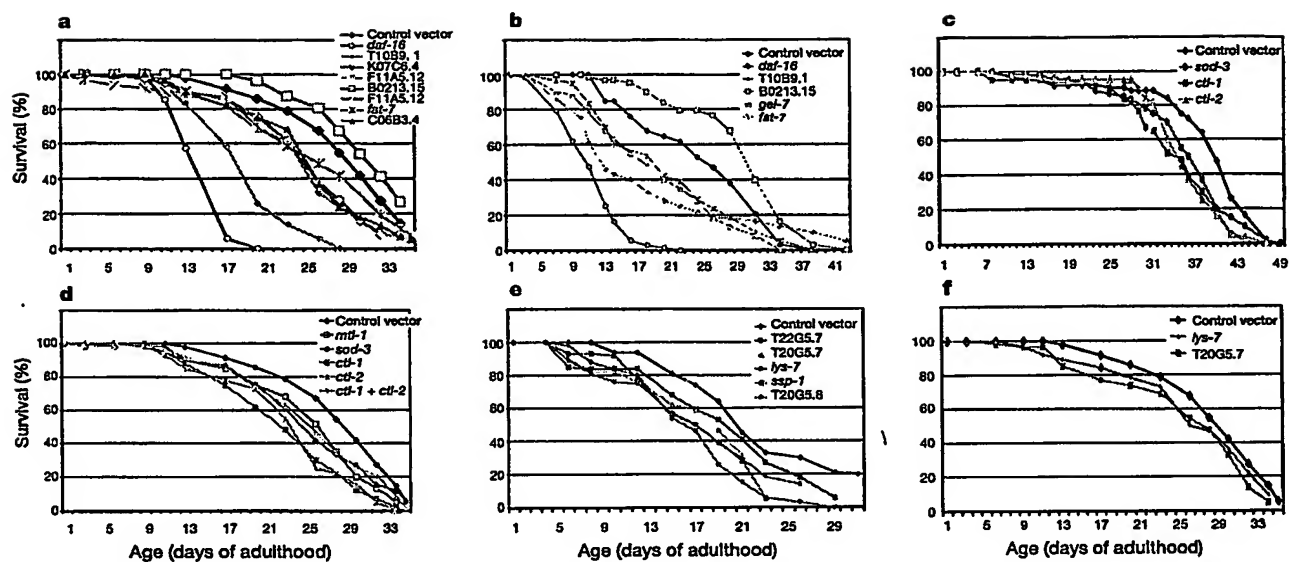
Figure 7



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Figure 8



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Figure 9

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Figure 10

